

# SCH- D (vicriviroc)



**Drug Class:** Entry and Fusion Inhibitors

## Drug Description

---

SCH-D, also known as SCH 417690 and vicriviroc, is a piperazine-based CCR5 receptor antagonist. [1]

## HIV/AIDS-Related Uses

---

SCH-D is a piperazine-based CCR5 antagonist currently in Phase II trials.[2] It is a novel, orally active entry and fusion inhibitor that holds promise for use in HIV infected patients who are resistant to enfuvirtide and other antiretrovirals.[3] SCH-D received fast-track approval status from the FDA in 2005.[4]

A Phase II trial in treatment-naïve patients was discontinued in October 2005 because detectable viral levels returned in some patients taking SCH-D and lamivudine/zidovudine compared to the control group taking efavirenz and lamivudine/zidovudine. No significant adverse events contributed to the discontinuation. Patients in this study will remain on SCH-D until alternate regimens are chosen with their physicians.[5]

A second Phase II trial in treatment-experienced patients will continue. The manufacturer also plans to continue evaluating SCH-D in combination with other treatment regimens in treatment-naïve and -experienced patients.[6]

## Pharmacology

---

Chemokine receptors expressed on the surface of immune cells are known to play a critical role in HIV infection and transmission. Entry and fusion inhibitors act differently than other classes of anti-HIV drugs (e.g., protease inhibitors, nucleoside reverse transcriptase inhibitors) by preventing HIV from infecting and entering cells, rather than trying to eradicate HIV after the virus has infected a cell. The CCR5 receptor acts with the CD4 receptor on the surface of T cells to facilitate entry of HIV into cells. Because previous research has suggested that individuals who lack a functional CCR5 receptor are largely resistant to HIV infection, the CCR5 receptor has been a target of investigation in development of anti-HIV therapy.[7]

SCH-D is a small-molecule inhibitor that binds to the cell's CCR5 receptor. When the drug binds to the CCR5 receptor, the receptor's conformation changes. This prevents HIV's gp120 protein from binding to CCR5 and consequently prevents the virus from entering the cell.[8]

SCH-D is similar to SCH-C, another CCR5 receptor antagonist developed immediately prior to SCH-D. Both compounds are orally bioavailable with potent in vitro activity against HIV. SCH-D has greater in vitro potency, with mean 90% inhibitory concentration (IC<sub>90</sub>) values approximately fivefold to tenfold lower than SCH-C. SCH-D was administered to HIV infected, treatment-naïve patients in three dosage groups (10 mg, 25 mg, 50 mg) and compared to placebo. Mean log<sub>10</sub> reductions in viral load were better compared to results of a similarly designed Phase I study of SCH-C, suggesting that SCH-D has greater in vitro and in vivo antiviral effects.[9]

SCH-D has been shown to be safe and well tolerated in Phase I trials. An additional Phase I study has been planned to evaluate the safety and efficacy of SCH-D, comparing the effects of three different doses of the drug in HIV infected patients taking concurrent antiretroviral therapy (ART).[10]

Phase I trial data in treatment-naïve HIV patients suggest that SCH-D's suppression of HIV viral load is dose-dependent. SCH-D does not appear to induce CYP3A4 and has an elimination half-life of approximately 24 hours.[11]

## Adverse Events/Toxicity

---

No drug-specific toxicity was identified in a small Phase I study in HIV infected, treatment-naïve patients; SCH-D was safe, well tolerated, and active at all dose levels tested in the study.[12] [13]

## Clinical Trials

---

For information on clinical trials that involve SCH-D (vicriviroc), visit the ClinicalTrials.gov web site at <http://www.clinicaltrials.gov>. In the Search box, enter: SCH-D (vicriviroc) AND HIV Infections.

# SCH- D (vicriviroc)



## Dosing Information

---

Mode of Delivery: Oral.[14]

Dosage Form: Phase I studies of SCH-D have evaluated 10 mg, 25 mg, and 50 mg tablets.[15]

## Other Names

---

SCH 417690[16]

Vicriviroc[17]

## Further Reading

---

Rusconi S, Scozzafava A, Mastrolorenzo A, Supuran CT. New Advances in HIV Entry Inhibitors Development. Curr Drug Targets Infect Disord. 2004 Dec;4(4):339-55. PMID: 15578975

Tagat JR, McCombie SW, Nazareno D, Labroli MA, Xiao Y, Steensma RW, Strizki JM, Baroudy BM, Cox K, Lachowicz J, Varty G, Watkins R. Piperazine-Based CCR5 Antagonists as HIV-1 Inhibitors. IV. Discovery of 1-[(4,6-Dimethyl-5-pyrimidinyl)carbonyl]-4-[4-{2-methoxy-1(R)-4-(trifluoromethyl)phenyl}ethyl-3(S)-methyl-1-piperazinyl]-4-methylpiperidine (Sch-417690/Sch-D), a Potent, Highly Selective, and Orally Bioavailable CCR5 Antagonist. J Med Chem. 2004 May 6;47(10):2405-2408. PMID: 15115380

Turpin JA. The next generation of HIV/AIDS drugs: novel and developmental anti-HIV drugs and targets. Expert Rev Anti Infect Ther. 2003 Jun;1(1):97-128. Review. PMID: 15482105

## Manufacturer Information

---

SCH-D (vicriviroc)  
Schering - Plough Corp  
2000 Galloping Hill Rd  
Kenilworth, NJ 07033-0530  
(800) 526-4099

## For More Information

---

Contact your doctor or an AIDSinfo Health Information Specialist:

- Via Phone: 1-800-448-0440 Monday - Friday, 12:00 p.m. (Noon) - 5:00 p.m. ET
- Via Live Help: [http://aidsinfo.nih.gov/live\\_help](http://aidsinfo.nih.gov/live_help) Monday - Friday, 12:00 p.m. (Noon) - 4:00 p.m. ET

# SCH- D (vicriviroc)



## References

---

1. Schering Plough - News and Media, "Schering-Plough Presents Clinical Data on CCR5 Receptor Antagonist at 9th Conference on Retroviruses and Opportunistic Infections." Available at: [http://www.schering-plough.com/schering\\_plough/news/release.jsp?releaseID=381316](http://www.schering-plough.com/schering_plough/news/release.jsp?releaseID=381316). Accessed 01/20/06.
2. Schering Plough - News and Media, "Schering-Plough Presents Clinical Data on CCR5 Receptor Antagonist at 9th Conference on Retroviruses and Opportunistic Infections." Available at: [http://www.schering-plough.com/schering\\_plough/news/release.jsp?releaseID=381316](http://www.schering-plough.com/schering_plough/news/release.jsp?releaseID=381316). Accessed 01/20/06.
3. Aidsmeds.com - SCH-D. Available at: <http://www.aidsmeds.com/drugs/vicriviroc.htm>. Accessed 01/20/06.
4. Natl AIDS Treatment Advocacy Project (NATAP) - FDA grants fast track designation to Schering-Plough's vicriviroc for HIV. Available at: [http://www.natap.org/2005/HIV/061705\\_03.htm](http://www.natap.org/2005/HIV/061705_03.htm). Accessed 01/20/06.
5. Schering Plough - News and Media, "Schering-Plough Discontinues Phase II Study of Vicriviroc in Treatment-Naive HIV Patients, Continues Phase II Study in Treatment-Experienced HIV Patients." Available at: [http://www.schering-plough.com/schering\\_plough/news/release.jsp?releaseID=774673](http://www.schering-plough.com/schering_plough/news/release.jsp?releaseID=774673). Accessed 01/20/06.
6. Schering Plough - News and Media, "Schering-Plough Discontinues Phase II Study of Vicriviroc in Treatment-Naive HIV Patients, Continues Phase II Study in Treatment-Experienced HIV Patients." Available at: [http://www.schering-plough.com/schering\\_plough/news/release.jsp?releaseID=774673](http://www.schering-plough.com/schering_plough/news/release.jsp?releaseID=774673). Accessed 01/20/06.
7. Schering Plough - News and Media, "Schering-Plough Presents Clinical Data on CCR5 Receptor Antagonist at 9th Conference on Retroviruses and Opportunistic Infections." Available at: [http://www.schering-plough.com/schering\\_plough/news/release.jsp?releaseID=381316](http://www.schering-plough.com/schering_plough/news/release.jsp?releaseID=381316). Accessed 01/20/06.
8. J Virol - 2003;77:5201-8
9. Conf Retroviruses Opportunistic Infect. - 11th, 2004. Abstract 140LB.
10. ACTG A5211 - Ver. 2.0
11. Clinical Care Options for HIV - SCH D, a CCR5 Inhibitor, Shows Potent Antiviral Activity in Treatment-naive Subjects. Available at: <http://clinicaloptions.com/hiv/conf/croi2004/cs/140lb.asp>. Accessed 01/20/06.
12. Natl AIDS Treatment Advocacy Project (NATAP) - SCH-D, CCR5 Receptor Inhibitor, New HIV Drug in New Class of Drugs. Available at: [http://www.natap.org/2004/CROI/croi\\_10.htm](http://www.natap.org/2004/CROI/croi_10.htm). Accessed 01/20/06.
13. ClinicalTrials.gov - Safety and Effectiveness of the Oral HIV Entry Inhibitor SCH 417690 in HIV Infected Patients. Available at: <http://clinicaltrials.gov/ct/show/NCT00082498>. Accessed 01/20/06.
14. Schering Plough - News and Media, "Schering-Plough Presents Clinical Data on CCR5 Receptor Antagonist at 9th Conference on Retroviruses and Opportunistic Infections." Available at: [http://www.schering-plough.com/schering\\_plough/news/release.jsp?releaseID=381316](http://www.schering-plough.com/schering_plough/news/release.jsp?releaseID=381316). Accessed 01/20/06.
15. Aidsmeds.com - SCH-D. Available at: <http://www.aidsmeds.com/drugs/vicriviroc.htm>. Accessed 01/20/06.
16. MeSH - Available at: <http://www.nlm.nih.gov/mesh/MBrowser.html>. Accessed 01/20/06.
17. Natl AIDS Treatment Advocacy Project (NATAP) - FDA grants fast track designation to Schering-Plough's vicriviroc for HIV. Available at: [http://www.natap.org/2005/HIV/061705\\_03.htm](http://www.natap.org/2005/HIV/061705_03.htm). Accessed 01/20/06.